Trend Watch

ANTIDEPRESSANTS IN BIPOLAR DISORDER

by Elisa F. Cascade; John Reites; and Amir H. Kalali, MD

Because of the potential to induce mania or rapid cycling, guidelines caution that antidepressants should be used conservatively in the treatment of bipolar disorder. To better inform psychiatrists on current practice patterns, this article presents data on the use of antidepressants and other regimens most commonly used to treat bipolar disorder.

METHODS

We obtained data on product treatment regimen from Verispan's Prescription Drug & Diagnosis Audit (PDDA) database from December, 2005, to November, 2006, for bipolar disorder as defined by ICD-9 diagnosis codes 294.4, 296.5, 296.6, and 296.7. PDDA captures data on disease state and associated therapy from 3,100 office-based physicians representing 29 specialties across the United States.

RESULTS

As seen in Figure 1, 42 percent of patients with bipolar disorder were treated with monotherapy, 42 percent were prescribed two agents, and 16 percetn received three or more agents. Although there are many products used to treat bipolar disorder, the most common categories included mood stabilizers (54%)(e.g., lithium and antiepileptics), antipsychotics (50%), and antidepressants (34%) (Figure 2). With respect to bipolar patients treated with antidepressants, 56 percent of antidepressants were used in combination with a mood stabilizer. An additional 27 percent of bipolar patients treated with antidepressants were prescribed the product in combination with an antipsychotic, and nine percent of patients were treated with antidepressant monotherapy.

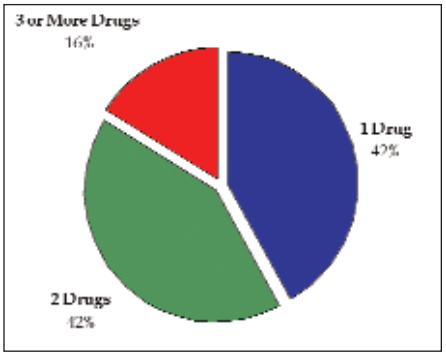

Figure 1. Treatment of bipolar disorder. Source: Verispan PDDA, ICD-9 Diagnosis 296.4, 296.5, 296.6, and 296.7, December 2005 to November 2006.

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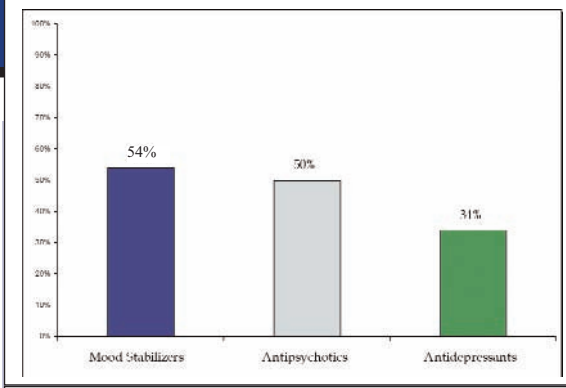

FIGURE 2. Products used to treat bipolar disorder. Mood stabilizers include antiepileptics and lithium. Source: Verispan PDDA, ICD-9 Diagnosis 296.4, 296.5, 296.6, and 296.7, December 2005 to November 2006.

EXPERT COMMENTARY—ANTIDEPRESSANTS IN BIPOLAR DISORDER

by Nassir Ghaemi, MD, MPH

The use of antidepressants in bipolar disorder is perhaps the most controversial topic in the treatment of bipolar disorder. Previously, clinical studies have indicated rather high rates of antidepressant use in bipolar disorder. In one study, for instance, about 80 percent of patients with bipolar disorder had been treated with antidepressants at some point, compared to only about 50 percent receiving mood stabilizers.[1] Further, when mood stabilizers are used, they are usually combined with antidepressants. This could be a problem since, if antidepressants have mood-destabilizing effects, they can counteract the benefits of mood stabilizers, thus leading to treatment nonresponse. In that same study, only about one-third of patients with bipolar disorder had ever been treated with mood stabilizers alone,[1] which means that only they had received a fair trial of a mood stabilizer (i.e., in the absence of an antidepressant). Other studies indicate that antidepressant use in academic centers tends to be somewhat lower than found in the community (about 50% vs 80% respectively),[2] and in some academic groups, like ours, where caution is exercised in using antidepressants, the rates of use are lower still (19% in our bipolar clinic).[3]

Until 2002, all bipolar treatment guidelines recommended antidepressant use as the first line treatment of bipolar depression. In that year, the APA treatment guidelines relegated them to second line use, after initial treatment with lithium or lamotrigine monotherapy.[4] This has led to marked protests, especially from some international groups,[5] with a response from American investigators.[6] The key concern that some of us have center on two issues: First, multiple, long-term, randomized studies have demonstrated lack of efficacy of antidepressants in prevention of depression in bipolar disorder, and no randomized data exist to the contrary;[7] second, some observational data, including the only available randomized studies, indicate that antidepressants appear to be associated with long-term worsening of the course of illness (mainly rapid-cycling) in about one-third of bipolar subjects.[6] Thus, our concern has been over long-term use in particular: If a drug is ineffective in most people and harmful in some, why use it? Considerations such as these have led to some awareness about risks with antidepressants in bipolar disorder, a caution that was almost nonexistent into the early 1990s.

These current practice data must be compared to other recently published pharmacy claims data (originally gathered in 2002–2003, compared to these data which are from 2005–2006). In the 2002–2003 data,[8] antidepressant monotherapy (which no one recommends) was the most common initial treatment given to patients with bipolar disorder (given to 50% of patients). Mood stabilizer monotherapy (lithium or anticonvulsants) was only given to about 25 percent of patients. Most patients in that community database initially received monotherapy, rather than polypharmacy, though eventually most patients ended up with polypharmacy.

In this database, the results appear somewhat more reassuring with mood stabilizers used more frequently than antidepressants, and the latter being used in only about one-third of the sample. Only nine percent received antidepressant monotherapy. It must be kept in mind that these data are a cross-sectional snapshot, whereas the other study above specifically examined initial new treatments given to previously untreated persons with bipolar disorder. If we put the two datasets together, it could be that clinicians initially start out on the wrong track, prescribing antidepressants alone as their most common treatment for bipolar disorder, and then, over time, they realize that they need to use mood stabilizers. Why there is this delay is unclear. Every textbook and treatment guideline recommends the reverse: Mood stabilizers need to be initiated at the beginning of treatment,

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with antidepressants only used in combination with mood stabilizers, or, as some of us prefer, relegated to later usage only if needed.

One final comment may be in order: Antipsychotics were used in this community database as much as mood stabilizers. Are antipsychotics mood stabilizers? I suggest not,[9] though this is also a matter of controversy.[10,11] One issue is clear: Clinicians and perhaps patients seem to be constantly searching for drugs other than mood stabilizers in the treatment of bipolar disorder, yet the evidence is hard to ignore that this illness does not improve without mood stabilizers at the core of any treatment regimen.[12]

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News from Mental Health America

Increased Suicide Rate in Children and Teens Found

by David Shern, PhD
President and CEO, Mental Health America

Data published in the February, 2007, issue of *Pediatrics* ("Annual Summary of Vital Statistics: 2005") measured death rates in youth. The findings indicated that the youth death rates did not change significantly between 2003 and 2004, but that suicides increased significantly between this period. For youth aged 14 to 19 the suicide rate increased by 11 percent, from 7.3 per 100,000 to 8.2 per 100,000. Similarly for youth aged 10 to 14, the rate increased by 8 percent, from to 1.2 to 1.3 per 100,000 (pediatrics.aappublications.org).

At a time when understanding of mental illnesses and their treatments is better than ever, an increased rate of suicide—an almost wholly preventable tragedy—is completely unacceptable. This is particularly true in light of the steady decline in suicide rates since the early 1990s. This is a disturbing reversal of progress.

While drawing conclusions related to the causes of this increase would be premature, it could be related to actions of the Food and Drug Administration. In 2004, the FDA mandated labeling for selective serotonin reuptake inhibitors (SSRI) antidepressant medications, after reviewing research that indicated a small increase in suicidal thinking—not actions—among young people taking the medications. It is important to note the distinction between suicidal thinking, self-injury, and fatal suicide: The FDA warns only of suicidal thoughts in its labeling; research does not indicate an increase in actual suicides.

As a result of the agency's activities, dramatic decreases in SSRI use in the teen population were noted [For additional information see: Cascade E, Kalali A. Update on trends in antidepressant use: Upswing in 2006 following period of decline. *Psychiatry 2006*;3(10):34–35]. Other research has indicated a general relationship between the use of SSRIs and decreasing suicide rates. One could, therefore, wonder if the FDA's actions and the subsequent decrease in access to these antidepressants have in fact caused an increase in youth suicide. It is, therefore, imperative that the federal government move aggressively to comprehend any potential consequences of their actions on the lives of youth.

There is nothing ambiguous about death as a consequence of illness. Ninety percent of suicides are attributable to a mental illness, most often depression, which affects one of every eight teens and one in 33 children. While not all children and adolescents living with depression need an antidepressant, for many these treatments can be an effective and even life-saving component of their treatment plan. The FDA's black box labeling on SSRIs and the media attention paid to this issue have created yet another formidable barrier to treatment for youth—by scaring young people and parents away from care and contributing to a decline in treatment. Without treatment, suicide is a real risk. Youth who need mental health treatment and go without it are at risk of the very outcome the agency aimed to prevent: suicide. The FDA and other federal agencies must take action to counteract any unintended consequences.

More research is needed to clearly understand the underlying root of any increase in the youth suicide rate, as well as to determine the affect of the black box on treatment utilization. As Mental Health America and other advocacy groups work with the FDA and other federal agencies, providers are in a key position to educate their communities on the inherent risks of untreated mental disorders and the importance of treatment and support for children and adults, as well as their families.

For more information, please visit www.mentalhealthamerica.net.